REMARKS

Status of the Claims

Claims 1-4 and 9-40 were withdrawn. Claims 5-8 were pending and examined in the October 23, 2006 Office Action. In this reply, claims 5-8 have been amended and new claims 41, 42, and 43 added. No new matter has been added. Accordingly, claims 5-8 and 41-43 will be pending upon entry of this amendment.

Claims 5, 7 and 8 have been amended to clarify the meaning of the abbreviation "GalNAc-transferase." Specifically, the full name, UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase, has been substituted for the abbreviation in the claims. Support for this amendment is found on page 3, lines 13-14 of the original specification.

Claim 6 has been amended to claim with more particularity the amino acid sequences that can comprise the lectin polypeptide. The claims have been amended to include the specific SEQ ID NOS of the amino acid sequences found in Table III. Support for this amendment is found in Table III (pages 59-66) of the original application and the Preliminary Amendment filed October 8, 2004.

New claim 41 covers an isolated lectin polypeptide consisting of a truncated mammalian UDP-GalNAc:polypeptide N-acetylgalactosaminyltransferase consisting of the amino acid sequences of SEQ ID NOS: 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, and 127 only. Support for this claim is found in Table III (page 59-66) of the original application and the Preliminary Amendment filed October 8, 2004.

New claims 42 and 43 cover the lectin polypeptides, GalNAc-T2 and GalNAc-T4, respectively, specifically used for the binding studies in Example 3 of the application. Support for these new claims is found in the original application in Table III (specifically page 60, lines 10-14 and page 61, lines 5-9), Example 3 (page 70, line 12- page 73, line 14), and the Preliminary Amendment filed October 8, 2004.

Claim Objections

Claims 5-8 are objected to because they recite the abbreviation "GalNAc-transferase" without defining it in the claim. The full name for the abbreviation has been substituted into the claims and it is respectfully submitted that claims 5-8, as currently drafted, overcome this objection.

Rejections under 35 U.S.C § 112, Second Paragraph

Claim 6, and claim 7 which depends therefrom, are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The Examiner contends that the phrase "amino acid sequences of GalNAc T1-T16 set forth in Table III herein" renders the claims vague and indefinite because it is not clear what specific amino acid sequences are being referred to in the claims. Claim 6 has been amended to substitute the list of specific SEQ ID NO identifiers for the phrase. Thus, it is respectfully submitted that claims 6 and 7 as amended are clear and meet the requirements of 35 U.S.C. § 112, second paragraph.

Rejections under 35 U.S.C § 112, First Paragraph for Lack of Written Description

Claims 5-8 are rejected under 35 U.S.C. § 112, first paragraph, for lack of written description. The Examiner contends that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one of skill in the art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, he contends that the claims are drawn to a genus of isolated lectin polypeptides of any amino acid sequence and structure consisting of any truncated mammalian GalNAc-transferase polypeptide comprising any domain selected from the group consisting of the lectin domain of any mammalian polypeptide GalNAc-transferase, any lectin-functional variant and fragments thereof. He further contends that the scope of this genus includes many members with differing nucleotide sequences and biological structure and is highly variable because a significant number of structural and biological differences between genus members exist. Lastly, he states that the application does not describe and define any structural features, amino acid sequences, and biological functions that are

commonly possessed by the members of the genus, as well as failing to provide a written description of representative members of the claimed genus. This rejection is respectfully traversed.

The test for compliance with the written description requirement is that the specification must contain sufficient information to persuade a person of ordinary skill that the inventor was in possession of the invention defined by the claims. *Vas-Cath, Inc. v. Mahurkar,* 935 F.2d 1555, 1563 (Fed. Cir. 1991). The specification as filed satisfies this test.

The application and claims as written disclose both unique functional and structural properties of the claimed lectin polypeptides. The claimed lectin polypeptides consist of a truncated mammalian GalNAc-transferase polypeptide consisting of a lectin domain or variants thereof, the function of which is fully described in the present specification. Specifically, the application sets forth that the lectin domains confer unique properties to the Gal-NAc-transferases including selective GalNAc-glycopeptide substrate specificity, as well as binding properties for peptides and carbohydrates to enhance catalytic properties, and other functions related to the O-glycosylation process. See application, page 9, lines 6-9. The specification further describes the function of the lectin domain of the GalNAc-transferases as the binding site for GalNAc and as providing a lectin-mediated chaperone-like function required for Golgi transport of O-glycosylated proteins (application, page 36, line 20- page 37, line 27). Thus, the specification describes biological functions that are commonly possessed by the lectin domains. Additionally, the claims themselves recite that the lectin domains have lectin binding activity.

The application as filed also describes common biological structures of the claimed genus, including amino acid sequences. Table III contains the amino acid and DNA sequence of sixteen lectin domains. See application, page 59, line 12-page 66, line 20. The disclosure of this number of species alone, in terms of DNA and amino acid sequence, would be sufficient to convey to a person of skill in the art that the inventors had possession of the genus. However, the application also discloses common structural characteristics of the lectin domain, including that this lectin domain region is approximately 130 amino acid sequences at the C-terminal end of the polypeptide, and exhibits similarity with the galactose binding lectin, ricin (application, page 49, lines 2-4).

Figure 1 sets forth that the lectin domain consists of three domains, α-,β-, and γ-ricin-like repeats. The figure also discloses conserved amino acid residues within the lectin domain. See Figure 1, application, page 11, lines 16-19. Moreover, Figure 2 discloses the multiple sequence alignment derived from the 16 lectin domain amino acid sequences. This Figure also discloses conserved motifs and residues. See application, Figure 2 and page 11, lines 21-25.

Additionally, the application sets forth the relation of the biological structure, *i.e.,* amino acid sequence, to the function of the lectin domains. Using multiple sequence alignment analysis, the applicants produced lectin domains of known amino acid sequence that bound specifically to GalNAc. See application, page 31, lines 6-16. Also with the use of the multiple sequence alignment analysis, the applicants "defined minimal sequences of functional lectin domains" that are set forth in Table III. See application, page 66, line 21.

The "functional variants" of the lectin domains are also described in the present application such that a person of skill in the art would recognize that the inventor had possession of these "functional variants" at the time of the filing of the application. These "functional variants" are described as those that contain an amino acid change which does not alter overall conformation and substrate specificity of the native polypeptide (application, page 21, lines 13-19).

The Examiner recognizes that Example 3 describes two specific truncated GalNAc-transferase lectins. However, he believes this description of two species is not enough to describe the genus. Applicants respectfully submit that this is incorrect. Example 3 fully describes the binding specificity of two specific truncated GalNAc-transferase lectins, whose structure, *i.e.*, amino acid sequence, is described in Table III (application, page 71, line 4-page 72, line 30 (Table IV)). As fully shown above, the present application describes both the function and the structure of the claimed genus. Moreover, the application sets forth the correlation between the structure and the function. This description combined with the complete description of two species is sufficient to describe the claimed genus. The application further states that the methods used in the Example to establish the binding activity of the two species of truncated lectins can be applied to all animal

and mammalian polypeptide GalNAc-transferase lectins with functional lectin domains. See application page 73, lines 1-14.

The Examiner citing *University of California v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997) states at page 4 of the Office Action:

> To fully describe the genus of genetic materials, which is a chemical compound, applicants must (1) fully describe at least one species of the claimed genus sufficient to represent said genus whereby a skilled artisan, in view of the prior art, could predict the structure of other species encompassed by the claimed genus and (2) identify the common characteristics of the claimed molecule, e.g. structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these.

Applicants respectfully submit that they have met this criteria for written description and one of skill in the art having read the specification of the present application would recognize that the inventors were in possession of the claimed genus at the time of filing the application. Two species are described fully in Example 3 in terms of binding activity and structure, *i.e.*, amino acid sequence. Moreover, the claimed genus is described in terms of biological function and structure, as well as the correlation between the two.

In summary, every claim feature of claims 5-8 is sufficiently described by the present specification. Claim 5 covers an isolated lectin polypeptide consisting of a truncated mammalian GalNAc-transferase polypeptide. Support for this claim feature is found in the application at page 1, lines 18-22; page 8, lines 1-4; page 11, lines 12-18; page 38, lines 15-16; Example 3, page 70, line 12-page 75, line 14; and Figure 1. The truncated GalNAc-transferase polypeptide comprises the lectin domain of mammalian polypeptide GalNAc-transferase, a lectin-functional variant or fragments thereof. This claim limitation is described on page 1, lines 18-24; page 8, lines 1-6; page 11, lines 12-2; page 21, lines 13-19; page 59, line 12-page 66, line 20; and Figures 1 and 2 of the

current application. Additionally, claim 5 calls for the lectin domain to have lectin binding activity. Support for this feature is found in the application as filed at page 9, lines 6-9 and page 36, line 20-page 37, line 27. Lastly, the claim recites that the truncated polypeptide not encompass the intact, functioning catalytic domain of the enzyme. This limitation is described in the application at page 28, lines 28-29.

Claims 6-8 depend from claim 5, and thus, recite all of the above limitations as well as additional features. Claim 6 covers a lectin polypeptide of claim 5 having the amino acid sequence selected from the amino acid sequences of SEQ ID NOS: 97, 99, 101, 103, 105, 107, 109, 111, 113, 115, 117, 119, 121, 123, 125, and 127. This feature is supported in the specification at page 59, line 12-page 66, line 20 and the Preliminary Amendment filed October 8, 2004. Claim 7 covers the lectin polypeptide of claim 6 further comprising 10-20 amino acid residues of the corresponding GalNAc-transferase sequence at its carboxy or amino terminus. Support for this claim limitation is found in the specification at page 66, lines 21-33. Lastly, claim 8 recites that the GalNAc-transferase polypeptide of claim 5 is human. Support for this additional feature is found throughout the specification, but specifically at page 8, line 5; page 8, line 10; page 26, line 20-page 28, line 14.

Thus, the present specification and claims fully meet the written description requirement in that every claim limitation is disclosed and described in the application as filed.

Rejections under 35 U.S.C § 112, First Paragraph for Lack of Enablement

Claims 5-8 are also rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner contends that the present specification is enabling for the truncated GalNAc-T2 and GalNAc-T4 lectins described in Example 3, but does not provide enablement for any other embodiments recited in the claims. See Office Action, page 4. This rejection is respectfully traversed.

The present specification contains all of the information that would be required by those skilled in the art to practice the invention defined by the present claims without undue

experimentation. An analysis of the *Wands* Factors (such as the quantity of experimentation necessary, the amount of guidance or direction, and the presence or absence of working examples) shows this to be the case. Example 3 provides a working example for two species. The example also provides guidance and direction for applying the methods in the example to other lectins, stating that the methods used to make lectin domains and use them in binding assays "... can be applied to all animal and mammalian polypeptide GalNAc-transferase lectins." See application, page 73, lines 2-3. See also page 38, lines 11-14. More guidance is provided for in the application with the description of the amino acid sequences of fourteen additional lectin domains, as well as the common characteristics of the structure of the lectin domains and the correlation of this structure to the disclosed lectin function. See specification at page 59, line 12- page 66, line 33, Figures 1 and 2.

Furthermore, the methods used in the application to make and use the truncated lectin polypeptides are well known in the art, and include the use of PCR (Example 1), production of recombinant proteins (Examples 1, 2 and 3), and use of the recombinant proteins in ELISA assays and other binding assays (Examples 2 and 3). Using the information regarding amino acid sequence and biological function disclosed in the specification and drawings along with techniques well-known to those skilled in the art (such as PCR and production of recombinant proteins), a person of ordinary skill in the art could make and use the invention defined by the present claims, and prepare isolated lectin polypeptides with a functional lectin domain, a lectin-functional variant, or a fragment.

The Examiner further contends that the it would be unpredictable and require undue experimentation to produce any truncated GalNAc-transferase polypeptide that does not have a catalytic domain but retains lectin binding activity. See Office Action, pages 4-5. Applicants respectfully disagree.

As fully discussed above, Figures 1 and 2 of the application describe the position of the lectin domain in relation to the catalytic domain of the GalNAc-transferase polypeptide and multiple sequence analysis was used to determined the borders between the two regions. See application,

page 59, lines 6-10. The lectin domain is about 130 amino acids at the C-terminal end. Moreover, the functions of the catalytic domain and the lectin domain are fully described in the application, such that a person of skill in the art could easily screen a truncated polypeptide for the requisite functions. Also, the structure of a number of lectin domains are disclosed in the application, as well as specific binding assays for lectin activity.

If this information were not enough, the application sets forth *specific methods* for producing polypeptide with functional lectin domains without the catalytic unit, such as expressing the lectin in a secreted soluble form which lacks the N-terminal tail, transmembrane sequence, stem region and catalytic unit. While the disclosed methods are "conventional expression systems familiar to those skilled in the art," they are nevertheless disclosed in the application. See application, page 28, line 29 – page 29, line 18. Moreover, Example 3 sets forth specific binding assays for the lectins which "utilize recombinant GalNAc-transferase lectins" and "excludes potential binding activity through the catalytic unit." See application, page 73, lines 10-14.

Thus, while some experimentation would be necessary to produce a truncated GalNAc-transferase polypeptide with a lectin domain only, it would not be undue. As shown, the application does more than give a "[g]eneral teaching regarding screening and searching" (Office Action, page 5): it provides specific guidance and examples that one of skill in the art along with known techniques, could use to produce any truncated GalNAc-transferase polypeptide as covered by the present claims. Given the disclosure of starting materials and specific methods to produce and use the desired polypeptides with functional lectin domains and no catalytic domain, the present specification provides more than a "plan" or "invitation to experiment", it provides specific guidance and specificity as to how to carry out the plan and is thus fully enabled. See *Enzo Biochem, Inc. v. Calgene, Inc.*, 188 F.3d 1362, 1374 (Fed. Cir. 1999).

In conclusion, claims 5-8 meet the enablement requirements of 35 U.S.C. § 112, first paragraph, and this rejection should be withdrawn.

CONCLUSION

In view of the above amendments and remarks, it is respectfully submitted that the pending claims are now in condition for allowance and such action is earnestly solicited. If the Examiner believes that a telephone conversation would help advance the prosecution in this case, the Examiner is respectfully requested to call the undersigned attorney at (212) 527-7631. The Examiner is hereby authorized to charge any additional fees associated with this response to our Deposit Account No. 04-0100.

Dated: January 22, 2007

Respectfully submitted,

By _____

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